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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,803	09/10/1999	MARGARET A. LIU	19188PCA	3309

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/393,803	LIU ET AL.
	Examiner	Art Unit
	Gerald G Leffers Jr., PhD	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-68 and 70-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *64-68,70-73 and 75-77* is/are allowed.

6)☒ Claim(s) *50-63 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment to the specification, filed 2/17/2004, in which a new paper copy of the sequence listing, CRF and attorney's statements were submitted. These documents have been entered into the file and the application is now in sequence compliance.

Receipt is also acknowledged of an amendment, filed 10/10/2003, in which claims were amended (claims 65 and 74) and in which claim 69 was cancelled. Claims 50-68, 70-77 are pending and under consideration in the instant application. This action is not final as new grounds of rejection are made herein that were not necessitated by applicants' amendment of the claims in the response filed 10/10/2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejected claims are directed to a polynucleotide which, upon *in vivo* introduction into a mammalian cell is non-replicating and which induces the co-expression of at least two gene products where the nucleic acid comprises at least two cistrons and where at least one of the cistrons encodes at least one immunogenic epitope of an HIV antigen. The claimed nucleic acids can comprise, optionally, at least two or at least three cistrons that are operatively linked to one or more promoter sequences and which can comprise operatively linked transcription termination

sequences for each cistron. There is no limitation in the claims as written as to what cell types *in vivo* the cells cannot be replicative. There is no limitation in the rejected claims as to under what conditions the immunogenic epitope is immunogenic. It is noted that the phrase "first cistron encodes a human immunodeficiency virus (HIV) gene...portions of pol not encoding a functional polymerase" from claim 51 can be reasonably read broadly to include any nucleic acid sequence encoding any part of the polymerase comprised within any other coding sequence (e.g. encoding any amino acid from within pol).

Claims 50-51 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldsmith et al (U.S. Patent No. 5,861,290; see the entire reference). **This is a new rejection.**

Goldsmith et al teach methods and polynucleotide constructs for treating host cells for infection or hyperproliferative disorders where the construct has a cis-acting regulatory sequence that is regulated by a trans-acting factor and an effector gene that renders the cell susceptible to protection or destruction (e.g. the Abstract). Goldsmith et al teach that suitable vectors for practicing their invention include replication defective retroviral particles or suitably non-pathogenic derivatives of replication-competent retroviral vectors(e.g. column 10, lines 43-50; Figures 1-3). For example, the specification teaches that recombinant retroviral vectors may also be formulated for *in vivo* administration if they are replication defective and include HIV-derived vectors (e.g. an HIV-based retroviral vector expressing the env gene obtained from HIV-1_{SF162}) (e.g. column 15, lines 20-45; claims 13-19).

The replication defective HIV-derived vectors taught by Goldsmith et al necessarily comprise multiple cistrons present within the vector that express multiple proteins in animal cells

in culture and which would reasonably be expected to express multiple gene products (e.g. $gp160^{env}$ and a selection marker) if introduced into at least some mammalian cell types *in vivo*. The skilled artisan would necessarily expect that the HIV proteins expressed by the replication defective vectors taught by Goldsmith et al would necessarily comprise at least one epitope that is immunogenic under at least some conditions (e.g. expression from an efficient high-copy eukaryotic vector in rabbits). It is further noted that for a circular replication-defective vector such as those taught by Goldsmith et al, all genes within the circular vector can be considered as "downstream" from one another.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 50-54, 74 are rejected under 35 U.S.C. 102(e) as being anticipated by Hu et al (U.S. Patent No. 6,107,062; see the entire patent). **This is a new rejection.**

Hu et al teach antisense viruses and antisense ribozyme viruses that comprise all of the structural genes of the virus from which they are derived, but which are also replication defective in that they lack the appropriate coding sequences for at least one essential trans element needed for viral replication (e.g. HIV tat). Exemplified embodiments include HIV genomes (e.g. HIV-

1IIIB) where the tat coding sequences have been reversed to provide an antisense sequence directed to tat coding sequences (e.g. column 12, lines 35-43).

Upon introduction *in vivo* into a mammalian cell lacking the complementing tat function such viral vectors taught by Hu et al would be nonreplicative, but would also be expected to express at least one of the HIV gene products as well as the tat antisense or ribozyme molecules (i.e. different gene products). The skilled artisan would necessarily expect that the HIV proteins expressed by the replication defective vectors taught by Hu et al would necessarily comprise at least one epitope that is immunogenic under at least some conditions (e.g. expression from an efficient high-copy eukaryotic vector in rabbits).

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-63 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claims 50 and 74 are vague and indefinite in that the metes and bounds of the phrase "A polynucleotide...comprising...optionally, a third cistron..." are unclear. The claims are unclear due to the open claim language "comprising" followed by "optionally, a third cistron". This arrangement makes it unclear the polynucleotide of the invention can have a *minimum* of two or three cistrons with the ability to have additional product-coding sequences, or if the claims are limited to nucleic acids having *at most* three cistrons. It would be remedial to amend the claim language to clearly indicate what is intended by the current claim structure.

Claim 54 is vague and indefinite in that it is impossible as the claim is currently written to determine if the different elements, and which elements, are claimed in the alternative. It would be remedial to amend the claim language to properly claim each of the different gene products in the alternative, clearly delineating what is intended for each alternative embodiment.

Conclusion

Claims 50-68, 70-77 are pending and under consideration in the instant application. Claims 50-63 and 74 are rejected herein. Claims 64-68, 70-73 and 75-77 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl

GERRY LEFFERS
PRIMARY EXAMINER